UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/020,482	10/30/2001	Edward M. Atkinson	226272003311	7120

25226 7590 10/03/2003

MORRISON & FOERSTER LLP
755 PAGE MILL RD
PALO ALTO, CA 94304-1018

EXAMINER	
HILL, MYRON G	

ART UNIT	PAPER NUMBER
1648	8

DATE MAILED: 10/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/020,482	ATKINSON ET AL.	
	Examiner	Art Unit	
	Myron G. Hill	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *47- 49, and 93- 124* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4,6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This action is on claims 47- 49 and 93- 124.

Information Disclosure Statement

A signed and initialed copy of IDS papers #4 and #6 are enclosed.

Priority

Objections to Claims

Claim 49 is objected to because of the following informalities: the word "claim" is misspelled. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 47- 49 and 93- 124 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In claims 47- 49, 93- 97, 101- 105, 114- 124 it is not clear what the metes and bounds of "stress or "sub-lethal stress" are and what specific parameters define them. In claims 47- 49, 93- 116 it is not clear what the metes and bounds of "about" is and what the comparative basis is for the 2 fold and what culture conditions are required. In claims 47- 49, 93- 98, and 100- 116 it is not

clear if this is in cell lysates or in the supernatants of unlysed cells. Claims 47, 93, and 117 are incomplete methods because they need a conclusion wherein a population of rAAV particles is generated. Claims 47 and 93 also require at least a step of generating/collecting virus.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 47- 49 and 93- 101, 103- 113 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shenk (US Pat 5,346,146) and Bantel-Schaal.

These claims are drawn to a method of producing rAAV particles under stress conditions.

Shenk discloses a method of producing a rAAV by cotranfecting producer cells having a heterologous DNA flanked by at least one inverted terminal repeat (ITR), helper AAV DNA coding one or more AAV packaging proteins needed for replication and encapsidation, and helper virus, in this case adenovirus (Column 12, lines 49- column 13, line 12). Shenk also teaches that AAV helper genes can be linked to a variety of promoters/and regulatory sequences including inducible promoters (columns 11-12), packaging genes can be stably integrated into the producer cell (column 12,

lines 6- 38) and introduction of rAAV vector can be done prior to infection, simultaneously to infection, or after infection (column 12, lines 60- 64).

Shenk does not teach culture under stress conditions.

Bantel-Schaal teaches about conditions in which AAV can be produced in cells. Bantel-Schaal teaches that stress can induce AAV proction. Figure 1 C shows an increase in viral DNA by up to or more than 20 fold and discloses that this correlates to 1.5- 2.8 fold increase when number of cells in the culture are adjusted for (page 263, column 2, line 9). The stress conditions taught by Bantel-Schaal are chemical (toxin), temperature, and radiation (UV). Bantel-Schaal also indicates that these stress conditions lead to delay of cell growth or growth retardation (page 261 column 2, RESULTS- page 262, column 1, line 8) and that DNA replication in cells cultured under stress conditions in the absence of helper is known (page 263, column 1, lines 8- 11) and that the stress induces more virus production (Figure 2).

Thus, one of ordinary skill in the art would have been motivated to stress conditions to produce more virus as taught by Bantel-Schaal because it would lead to increased rAAV production even in the absence of helper. One of skill in the art would know that culture conditions that induce growth arrest/retardation in cultured cells includes deficient media, no serum in cell culture for cells not adapted for such growth

It would have been *prima facie* obvious to grow rAAV of Shenk under the conditions of Bantel-Schaal to inclrease viral yield to generate a population of rAAV particles with the expectation of success.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 47- 49 and 93, 94, and 96 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 126 and 159- 162 of Allowed U.S. Patent Application No. 09/526,333. Although the

conflicting claims are not identical, they are not patentably distinct from each other because AAV is cultured under osmotic sub-lethal stress and not lysed.

In *Gerber Garment Technology Inc. v. Lectra Systems Inc.*, 16 USPQ2d 1436, the Court of Appeals Federal Circuit ruled that the prohibition of Double Patenting after Restriction is not absolute, and double patenting protection of section 121 does not apply where the claims have been changed in material respect from the restriction requirement. Reviewing the prosecution history in parent application 09/526,333, the restriction between groups III and VII was made on the basis that group III involved a method to purify rAAV using cationic and anionic chromatography, while group VII involved releasing rAAV from cells. However, during prosecution of elected group VII in application 09/526,333, at least one claim was changed in material respect, in that the group VII feature of purifying AAV from the supernatant without a lysis step using anion and cation chromatography, resulting in allowed claim 126. Since patent claim 126 was not consonant with the original restriction requirement, and since the instant claims are drawn to obvious embodiments encompassed by allowed claims 126 and 159- 162, a double patenting rejection is proper.

Claims 47- 49 and 93, 94, 96, 117 and 118 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 118 of copending Application No. 10/016767. Both sets of claims are drawn to a method of generating a population of rAAV by culturing the producer cells under sub-lethal stress. Because of the open language of the instant claims, they encompass

material included the copending claim 118. The limitation of the cancelled claim 117 in the other application has been included in claim 118.

This is a provisional obviousness-type double patenting rejection.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Myron G. Hill whose telephone number is 703-308-4521. The examiner can normally be reached on 9am-6pm Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4247. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Myron G. Hill
Patent Examiner
September 29, 2003

JAMES HOUSEL 10/1/03
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600